

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
5 July 2001 (05.07.2001)

PCT

(10) International Publication Number
WO 01/48021 A1

(51) International Patent Classification⁷: C08B 11/193, A61K 7/06

(74) Agent: PACCIONE, Stanley, J.; Union Carbide Chemicals & Plastics Technology Corporation, 39-Old Ridgebury Road, Danbury, CT 06817-0001 (US).

(21) International Application Number: PCT/US00/35615

(22) International Filing Date:
28 December 2000 (28.12.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/173,454 29 December 1999 (29.12.1999) US

(71) Applicant (for all designated States except US): UNION CARBIDE CHEMICALS & PLASTICS [US/US]; Technology Corporation, 39 Old Ridgebury Road, Danbury, CT 06817-0001 (US).

(81) Designated States (national): AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(72) Inventor; and

(75) Inventor/Applicant (for US only): GRUBER, James, Vincent [US/US]; 96 N. Middaugh Street, Somerville, NJ 08876 (US).

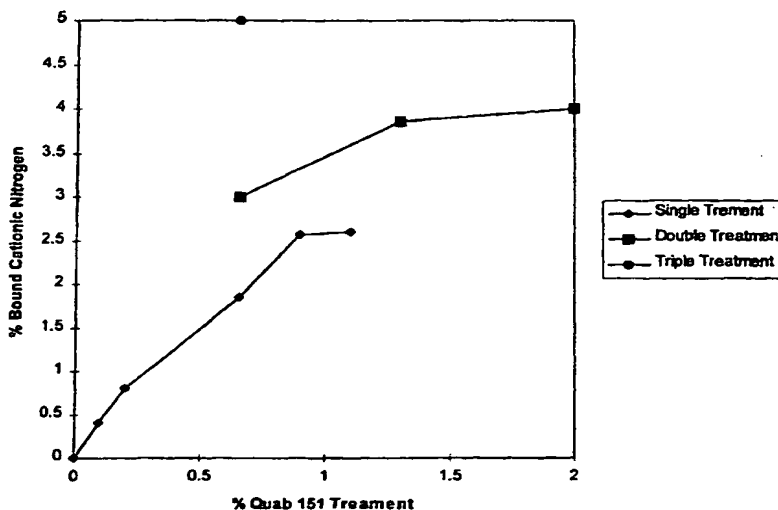
Published:

— With international search report:

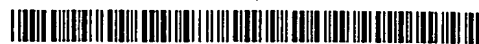
[Continued on next page]

(54) Title: HIGHLY CHARGED CATIONIC CELLULOSE ETHERS

Percent bound nitrogen verses percent epoxide treatment level for single (◆, EXAMPLES 1-5), double (■, EXAMPLES 6-8) and triple (●, EXAMPLE 9) treatments with 70% aqueous QUAB 151.



(57) Abstract: Highly charged cationically modified cellulose ethers having cationic substitution levels of at least about 3.0 wt.% are disclosed. The cationically modified cellulose ethers are useful, for example, in personal care formulations, e.g., shampoo. Methods for manufacturing the cellulose ethers are also disclosed.



— Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

HIGHLY CHARGED CATIONIC CELLULOSE ETHERS

Field of the Invention

The present invention generally relates to cellulose ethers and more specifically relates to cellulose ethers which are water-soluble and highly substituted with cationic substituents and methods for their preparation.

BACKGROUND OF THE INVENTION

Water-soluble cellulose ethers have been employed in a wide variety of applications, such as, for example, in personal care applications such as pharmaceutical and cosmetic compositions, and industrial applications such as viscosity adjusters, suspension aids, oil field drilling and fracturing materials and adhesion promoters.

Cationic modification of cellulose ethers is desirable particularly when the cellulose ethers are used in personal care applications, e.g., for enhanced substantivity to skin and hair. Such cationic modification is also desirable for pharmaceutical applications, e.g., especially in applications requiring mucoadhesion such as eye medication and buccal drug delivery systems. Cationic modification is also desirable for certain industrial applications, e.g., flocculation of fines in water treatment, binders in paper manufacturing and

adhesion promotion to siliceous materials, all of which are affected by the substantive properties of the polymer.

Methods for manufacturing water-soluble, cationic cellulose ethers are well known in the industry. Generally speaking, these methods involve reactions which are multi-phased. Typically, for example, the reactions will occur in such a fashion that the cellulose ether is slurried into an aqueous liquid which is a non-solvent for the cellulose ether where it reacts with a cationic reagent to afford the water-soluble, cationic cellulose ether. While attempts have been made to manufacture highly-charged cationic cellulose ethers, the methods employed typically involved the use of water immiscible organic solvents which are typically volatile components, can be toxic and are thus undesirable. Alternatively, proposed methods involved a reaction in a dry state where the cellulose ether is reacted with the cationizing reagent under substantially dry, i.e., no solvent, conditions and generally require an inorganic flow aid material, such as, for example, silica gel to aid in mixing. One difficulty with such dry methods generally lies in the ability to adequately purify the final product because of the presence of the added flow aid agent. Purification often cannot be accomplished without the use of washing solvents which essentially defeats the purpose of preparing the polymer in a dry state.

When cationic cellulose ethers are made in a multi-phased slurried fashion, the reaction typically requires addition of the cationic reagent as a liquid product. One common cationizing reagent sold commercially is glycidyltrimethylammonium chloride, also known in the art as (2,3-epoxypropyl)trimethylammonium chloride, which is commercially available as a 70 weight percent ("wt. %") aqueous solution, i.e., 70 wt. % cationic reagent ("solids"). Interestingly, under the typical multi-phase slurry reaction conditions employed to make cationic cellulose ethers, when the aqueous cationizing reagent is used to cationize the cellulose ether, an interesting phenomena occurs. That is, as the treatment level of cationizing reagent exceeds about 1.0%, the amount of cationic reagent which actually reacts with the polymer levels off. This phenomena creates a problem in the industry by limiting the amount of cationic substituent which can be derivatized onto the cellulose ether. More specifically, as the cationic reagent is added to the reaction, water is also added which ultimately dilutes the aqueous non-solvent reaction medium to the point that reaction efficiencies level off. It is unavoidable to add this additional water because it is present in the aqueous cationic reagent. Furthermore, the continued addition of aqueous reagent in an attempt to increase the cationic charge introduces more water into the reaction medium. The increased amount of water promotes the dissolution of the polymer

which often yields a gooey, intractable mass of polymer. Although increasing the solids concentration of the cationic reagent, e.g., to 90 wt. % solids, may help alleviate the problem, such products are generally not commercially available, presumably due to difficulties in manufacturing and handling such products. As a result of this dilution phenomena, cationic cellulose ethers of greater than 2.2% cationic substituent, e.g., nitrogen, have not been available.

However, cationic cellulose ether with higher cationic charges, e.g., at least about 3.0 wt %, can provide enhanced substantive properties relative to cellulose ethers with lower cationic charge levels. There exists, therefore, a need for such highly charged cationic cellulose ethers and a method to manufacture such cellulose ethers using common aqueous cationic reagents, e.g., 70 wt % solids, typical reaction solvents and standard reaction equipment. Such new cationic cellulose ethers may be useful in a variety of applications.

SUMMARY OF THE INVENTION

In accordance with the present invention, highly substituted cationic cellulose ethers are provided. The cellulose ether derivatives of the present invention can be manufactured having at a substitution level of at least about 3.0 wt % cationic substituent, for example, using commonly available aqueous cationic reagents, e.g., 70 wt % solids.

The methods involve the sequential reaction of cellulose ethers with the aqueous cationic reagents whereby water is removed between reaction steps. Advantageously, the cationic cellulose ethers can be prepared, in standard commercial equipment, using the multi-phase slurry technology, preferably without the use of flow aids. Quite surprisingly, it has been found that these can be highly charged, cationic cellulose ethers of the present invention can have rheological and performance properties which are unexpectedly different and often superior to the cellulose ethers of lower cationic charge, especially in personal care formulations.

DETAILED DESCRIPTION OF THE INVENTION

Cellulose ethers suitable for use in accordance with the present invention include etherified derivatives of cellulose. Typical cellulose ethers include for example, hydroxyethyl cellulose, hydroxypropyl cellulose, methyl cellulose, hydroxypropyl methyl cellulose, hydroxyethyl methyl cellulose, carboxymethyl cellulose, hydroxyethyl carboxymethyl cellulose and the like. Preferred cellulose ethers include hydroxyethyl cellulose and hydroxypropyl cellulose. Cellulose ethers such as those described above are readily commercially available. Alternatively, such cellulose ethers can be prepared from cellulose by methods known to those skilled in the art.

Ether substituents suitable for use in accordance with the present invention comprise ethers preferably having 2 to 4 carbon atoms per molecule. Typically, the ether substituent is derivatized onto the cellulose by reacting the cellulose with an alkylene oxide such as ethylene oxide, propylene oxide or butylene oxide, preferably ethylene oxide. The amount of ether substitution is typically from about 1.5 to 6 and preferably from about 2 to 4 moles of ether substituent per mole of cellulose ether. Further details concerning the manufacture of such cellulose ethers are known to those skilled in the art.

The molecular weight of the cellulose ethers suitable for use in accordance with the present invention typically ranges from about 10,000 to 2,000,000 grams per gram mole and preferably ranges from about 80,000 to 1,500,000 grams per gram mole. As used herein, the term "molecular weight" means weight average molecular weight. Methods for determining weight average molecular weight of cellulose ethers are known to those skilled in the art. One preferred method for determining molecular weight is low angle laser light scattering. The viscosity of the cellulose ethers typically ranges from about 5 to 6000 centipoise, preferably from about 100 to 3000 centipoise. Unless otherwise indicated, as used herein, the term viscosity refers to the viscosity of a 1.0 weight percent aqueous solution of polymer measured

at 25°C with a Brookfield viscometer. The average particle size of the cellulose ethers is not critical, but is preferably from about 0.01 to 1000 microns and more preferably from about 50 to 400 microns.

The ionic nature of the cellulose ethers of the present invention is not critical. The charge can be cationic, anionic, amphoteric or nonionic. It is typically preferred, however, that the ionic charge be cationic, anionic and more preferably nonionic. Those skilled in the art will recognize that if the starting cellulose ether is anionic, the resulting reaction product upon treatment with the cationizing reagent is actually an amphoteric polymer, containing both anionic and cationic species on the same cellulose ether backbone. Further details concerning the substituents and methods for modifying the ionic character of cellulose ethers are known to those skilled in the art.

In addition, the cellulose ethers may be derivatized with other substituents, e.g., hydrophobically-modified. Hydrophobic substituents suitable for use in accordance with the present invention comprise an alkyl or arylalkyl group having about 8 to 18 carbon atoms, preferably from about 10 to 18 carbon atoms and more preferably from about 12 to 15 carbon atoms. As used herein, the term "arylalkyl" group means a group containing both aromatic and aliphatic structures. Many hydrophobe-containing reagents suitable for use as hydrophobic substituents are commercially available and resulting hydrophobically-

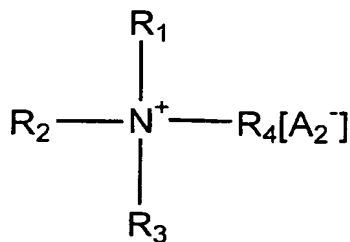
modified cellulose ethers are known as well such as disclosed in U.S. Pat. Nos. 4,228,277, 4,663,159 and 4,845,175.

The cationic cellulose ether derivatives of the present invention are water-soluble. As used herein, the term "water-soluble" means that at least 1 gram, and preferably at least 2 grams of the cellulose ether derivatives are soluble in 100 grams of distilled water at 25°C and 1 atmosphere. The extent of water solubility is control by the level of substituent groups, including the cationic groups, attached to the cellulose derivative. Techniques for varying the water solubility of cellulose ethers are known to those skilled in the art.

Typically, the cationic substituents suitable for use in the present invention comprise nitrogen. Preferably the cationic substituents are selected from the group consisting of alkyl substituted nitrogen compounds, aryl substituted nitrogen compounds or alkyl-aryl substituted nitrogen compounds. Often, the cationizing reagents used to provide the cationic substituents are alkyl substituted nitrogen halides such as, for example, (2,3-Epxoypropyl) trimethyl ammonium chloride available as a 70 wt % solids solution from Degussa Corporation as QUAB™ 151.

Preferably, the cationic substituents suitable for use in accordance with the present invention have the formula:

-9-



where;

each R_1 , R_2 , and R_3 is CH_3 or C_2H_5 ;

R_4 is $CH_2CHOHCH_2$ or CH_2CH_2 ; and

A_2 is a halide ion.

Preferably, R_1 , R_2 , and R_3 are CH_3 . Preferably, R_4 is $CH_2CHOHCH_2$. Chlorine is a preferred halide ion. Other cationic substituents may also be used in accordance with the present invention. In addition, R_1 , R_2 , or R_3 can also be an alkyl or arylalkyl group having about 8 to 18 carbon atoms.

Preferably, the substitution level of the cationic substituents on the cellulose ethers of the present invention ranges from about 3.0 to 8.0 wt % of the cationic substituent, e.g., cationic nitrogen based on the total weight of the cellulose ether. More preferably, the percent cationic nitrogen for the cationic cellulose ethers of the present invention is from about 3.0 to 6.0 wt %. Most preferably, the percent cationic substituent is from about 3.0 to 5.0 wt %. As used herein, percent cationic substituent is the percentage of cationic substituent covalently bound to the anhydroglucose monomers of the cellulose

-10-

ether. The substitution level can be determined by a number of different methods known to those skilled in the art. For example, a particularly preferable method for determining percent cationic nitrogen is the Kjeldahl method as disclosed in *Organic Analysis, volume III*. [Interscience Publishers, New York], pp., 136-141.

Determining the amount of covalently bound nitrogen can be accomplished, for example, by dialyzing the derivatized polymer against distilled water using dialysis membranes such as those supplied by the Spectrum company, Houston, Texas. Dialysis allows for the removal of the unreacted, low molecular weight nitrogen containing species and provides derivatives which contain only nitrogen reacted to the polymer. In addition, the level of covalent cationic substituent can be determined by nuclear magnetic resonance spectroscopy (NMR), the use of which is known to those skilled in the art.

Typically, the cationically-modified cellulose ethers of the present invention are prepared by: (i) reacting a cellulose ether with a first aqueous cationizing reagent to form a first reaction product comprising a first cationic cellulose ether and water; (ii) removing at least a portion of the water from the first reaction product, e.g., by centrifuging, to form a dried reaction product comprising the first cationic cellulose ether; and (iii) reacting the dried reaction product

with a second aqueous cationizing reagent to form a second reaction product comprising a second cationic cellulose ether having a higher substitution level of cationic substituent than the first cationic cellulose ether. Typically, the first cationic cellulose ether has a substitution level of less than about 2.5 wt % of the cationic substituent based on the total weight of the cellulose ether. The first cationizing agent and the second cationizing agent can be the same or different. Also, typically the dried reactor product comprises from about 0.1 to 50 wt % water based on the total weight of the dried reaction product.

In one aspect of the present invention, the highly substituted cationic cellulose ether derivatives of the present invention are formed in a sequential series of reaction steps substantially free of any type of inorganic flow aid materials, such as, for example, silica gel, in which the final product from the preceding reaction becomes the starting material for the next reaction. As used herein, the term "substantially free" means less than about 5 wt %, preferably less than about 2 wt % and more preferably less than about 1 wt % inorganic flow aid material based on the total weight of the cationic cellulose ether and the inorganic flow aid material. Such reactions could, in theory, be continued for many multiple sequential steps. However, for practical purposes, it is reasonable to expect that adequate substitution of the

cationic cellulose ethers of the present invention can be accomplished in two sequential steps. Thus, a cellulose ether is typically treated in one sequential step with a measured amount of the cationizing reagent, the product is isolated and this product becomes the starting material for the next sequential reaction. In this fashion, 70 wt % aqueous cationic reagent, for example, can be used without adverse interference with reaction efficiency at higher substitution levels. As an alternative to the initial sequential reaction described above, one of the commercially available cationic cellulose ethers with a lower substitution level, e.g., about 2 wt % cationic nitrogen, can be used as the starting material. Such cationic cellulose ethers are available, for example, from Amerchol Corporation under the tradename UCARE® Polymer. Particularly preferred for the purposes of the present invention are UCARE® Polymers JR-400 and JR-30M which both contain about 2.2 wt % cationic nitrogen.

In addition, surprisingly it has been found that the sequential manufacture of the cationic cellulose ethers of the present invention can be effective to prevent the amount of the aqueous non-solvent from increasing to the point where dissolution of the cationic cellulose ether product begins to occur. Efforts to obtain the highly substituted cationic cellulose ethers of the present invention in a single step by addition of large quantities aqueous 70 wt % cationic reagent often

-13-

converts the product into a highly swollen, gooey, intractable mass which can not be isolated using standard filtration equipment. It has also been surprisingly found that substituting the cationic cellulose ethers of the present invention with levels of cationic nitrogen greater than 3.0 percent can have unusual effect on the aqueous solution viscosity of the resulting cationic cellulose ethers.

A preferred end-use for cationic cellulose ether derivatives of the present invention is as a component in personal care compositions which comprise the cellulose ether derivative and a personal care ingredient. As used herein, "personal care ingredient" includes, but is not limited to, active ingredients such as for example, spermicides, virucides, analgesics anesthetics, antibiotic agents, antibacterial agents, antiseptic agents, antidandruff agents, vitamins, corticosteroids, antifungal agents, vasodilators, hormones, antihistamines, autacoids, kerolytic agents, antidiarrhea agents, anti-alopecia agents, anti-inflammatory agents, glaucoma agents, dry-eye compositions, wound healing agents, anti-infection agents, and the like, as well as solvents, diluents and adjuvants such as, for example, water, ethyl alcohol, isopropyl alcohol, higher alcohols, glycerine, propylene glycol, sorbitol, preservatives, surfactants, propellants, fragrances, essential oils, viscosity adjusters and the like. Such

personal care ingredients are commercially available and known to those skilled in the art.

The amount of the cellulose ether derivatives present in the personal care composition will vary depending upon the particular care compositions. Typically, however, the personal care compositions will comprise from about 0.1 to 99 weight percent of the cellulose ether derivative of the present invention. Often, the concentration of the cellulose ether derivative in the personal care composition will range from about 0.2 to 50 weight percent, and more often from about 0.5 to 10 weight percent based on the personal care composition.

Typical cleansing systems may contain, for example, water and a surfactant, like ammonium lauryl sulfate and ammonium laureth sulfate and, auxiliary surfactants like lauramide DEA or cocobetaines, thickening agents like NaCl, hydroxypropyl cellulose or PEG-120 methyl glucose dioleate, conditioners like Dimethicone, Polyquaternium-10 and, or PEG-2M polyethers, pH adjusters like citric acid or triethylamine and a chelating agent like tetrasodium EDTA. Likewise, bar soaps may contain, for example, surfactants like tallowate or cocoate and a feel modifier like glycerin.

Typical aerosol and non-aerosol hairsprays may contain, for example, a solvent like a low molecular weight alcohol and, or water, a propellant like dimethylether or a hydrocarbon, a resin like

poly(vinylpyrrolidone)/vinyl acetate copolymer, poly(vinylmethacrylate)/methacrylate copolymer, or a latex dispersion of polymers, a plasticizer like dimethicone copolyol and a neutralizing agent like aminomethyl propanol.

Typical creams may contain, for example, an oil like mineral oil, water, an emulsifier like methyl glucose sesquistearate or PEG-20 methyl glucose sesquistearate, a feel modifier like isopropyl palmitate or PEG-20 methyl glucose distearate, a polyhydric alcohol like methyl gluceth-20 and a stabilizer like carbomer.

Typical mousses may contain, for example, a solvent like water and, or alcohol, a surfactant like oleth-10, a feel modifier like isopropyl palmitate and a resin like polyquaternium-10 or poly(vinylmethacrylate)/methacrylate copolymer.

Typical gels may contain, for example, a viscosifying agent like carbomer, a solvent like water and, or alcohol, a styling resin like poly(vinylmethacrylate)/vinylmethacrylate copolymer, a neutralizing agent like aminomethyl propanol and a feel modifier like methyl gluceth-20.

Typical ophthalmic compositions, such as, for example, synthetic tears, ophthalmic lubricants, or pharmaceutical containing delivery systems, are neutrally buffered and isotonic. Levels of isotonic salts of up to about 0.9 parts by weight and up to 5 parts of the active

ingredient are often included. Typical inorganic isotonic ingredients include, for example, sodium chloride, boric acid, borax, etc., while typical natural isotonic ingredients include sugars such as dextrose, mannitol and sorbitol or polymeric sugars such as, for example, hyaluronic acid. The pH of these solutions can vary widely from 3 to 9 and is typically from about 6 to 8. Other common ophthalmic additives include, for example, viscosity adjusters, e.g., hydroxyethyl cellulose, propylene glycol, glycerols, carbonates and bicarbonates and ethylenediaminetetraacetic acid (EDTA).

Further details concerning the ingredients, amounts of ingredients and preparation methods of personal care compositions such as described above are known to those skilled in the art.

It has been surprisingly found that the highly charged cationic cellulose ethers of the present invention have unusual solubility properties in a typical surfactant shampoo formulation when compared to their corresponding lower charged derivatives of comparable molecular weight. More specifically, it has been found that when the highly charged cationic cellulose ethers of the present invention are dissolved into water and mixed into a shampoo surfactant mixture containing ammonium lauryl sulfate, sodium lauryl ether sulfate and cocamidopropylbetaine the formulation becomes nearly opaque,

whereas the low charged cationic cellulose ethers known in the art provide clear formulations.

Without being bound by theory, it is believed that the opaque nature of the polymer/surfactant mixture may be related to the development of a coacervate phase in the surfactant solution. Coacervate formation is dependent upon a variety of criteria such as molecular weight, concentration, and ratio of interacting ionic materials, ionic strength (including modification of ionic strength, for example, by addition of salts), charge density of the cationic and anionic species, pH, and temperature. Coacervate systems and the effect of these parameters have been described, for example, by J. Caelles, et al., "Anionic and Cationic Compounds in Mixed Systems", *Cosmetics & Toiletries*, Vol. 106, April 1991, pp 49-54, C. J. van Oss, "Coacervation, Complex-Coacervation and Flocculation", *J. Dispersion Science and Technology*, Vol. 9(5,6), 1988-89, 561-573, and D. J. Burgess, "Practical Analysis of Complex Coacervate Systems", *J. of Colloid and Interface Science*, Vol. 140, No. 1, November 1990, pp 227-238, which descriptions are incorporated herein by reference.

It is believed to be particularly advantageous for the cationic polymer to be present in a shampoo in a coacervate phase, or to form a coacervate phase upon application or rinsing of the shampoo to or from the hair. Complex coacervates are believed to more readily deposit on

-18-

the hair as suggested, for example, in PCT WO 98/18434 published October 1997. Thus, in general, it is preferred that the cationic polymer exist in the shampoo as a coacervate phase or form a coacervate phase upon dilution. If not already a coacervate in the shampoo, the cationic polymer will preferably exist in a complex coacervate form in the shampoo upon dilution with water

Techniques for analysis of formation of complex coacervates are known in the art. For example, microscopic analysis of the shampoo compositions, at any chosen stage of dilution, can be utilized to identify whether a coacervate phase has formed. Such coacervate phase will be identifiable as an additional emulsified phase in the composition. The use of dyes can aid in distinguishing the coacervate phase from other insoluble phase dispersed in the composition.

The characteristics of the opaque shampoos provides these shampoos with new and unexpected cosmetically significant properties. For example, it has been found that hair tresses treated with shampoos containing a commercially available cationic cellulose ether and one containing a highly charged variant made by the method of the present invention that is of comparable molecular weight shows improvements in wet-combing force reductions and detangling when compared to either the simple shampoo base without cationic polymer or a similar shampoo made with the lower charged

cationic cellulose of comparable molecular weight. Methods for measuring combing force are known to those skilled in the art.

Likewise, it has been surprisingly found that hair tresses treated with similar shampoos containing a highly charged cationic cellulose polymer that are curled and dried and subsequently tested for curl retention using standard methods known to those skilled in the art show improvements in curl retention when compared to tresses treated with either the simple shampoo base or with a shampoo containing a cationic cellulose ether of comparable molecular weight but lower cationic charge.

In addition, the cationic cellulose ethers of the present invention, because of their higher charge, may find applications as mucoadhesives in buccal drug delivery systems and as agents useful in microencapsulation as part of a polyelectrolyte complex. Polymers useful as mucoadhesives must have substantivity for the mucous membranes such as those lining, for example, the mouth, nose, vaginal and rectal regions of the body. As part of a polyelectrolyte complex, the highly charged cationic cellulose derivatives of the present invention will typically be complexed with a complimentary anionic polymer such as, for example, alginic acid or xanthan. Such complexes may take a variety of forms, but most typically will occur as, for example, sheets,

foams and microcapsules in which the active therapeutic ingredient is embedded within the polyelectrolyte complex matrix.

Further details concerning the ingredients, amounts of ingredients and preparation methods of mucoadhesive compositions and polyelectrolyte complexes such as described above are known to those skilled in the art.

EXAMPLES

The following examples are provided for illustrative purposes and are not intended to limit the scope of the claims which follow.

The following ingredients were used in the Examples.

UCARE® Polymer JR-400-cationic hydroxyethyl cellulose with a molecular weight of approximately 400,000, derivatized with approximately 1.8 percent cationic nitrogen. Available from Amerchol Corporation, Edison, NJ.

UCARE® Polymer LK-400- cationic hydroxyethyl cellulose with a molecular weight of approximately 400,000, derivatized with approximately 0.5 percent cationic nitrogen. Available from Amerchol Corporation, Edison, NJ.

UCARE® Polymer LR-400- cationic hydroxyethyl cellulose with a molecular weight of approximately 400,000, derivatized with

-21-

approximately 1.0 percent cationic nitrogen. Available from Amerchol Corporation, Edison, NJ.

UCARE® Polymer JR-30M-cationic hydroxyethylcellulose with a molecular weight of approximately 900,000, derivatized with 1.8-2.2 percent cationic nitrogen. Available from Amerchol Corporation, Edison, NJ.

QUAB® 151-Glycidyltrimethylammonium chloride available as a 70% aqueous solution. Available from Degussa, Ridgefield Park, NJ.

2-Propanol-Available from Fisher Scientific, Fair Lawn, NJ.

CELLOSIZ® QP-4400-Hydroxyethyl cellulose of approximately 400,000 molecular weight. Available from Union Carbide Corporation, Danbury, CT.

Acetic acid-Available from Aldrich Chemical Co., Milwaukee, WI.

Hair Tresses-Virgin Brown, and Bleached Blond tresses available from DeMeo Brothers, New York, NY.

EXAMPLES 1-5 **PREPARATION OF CATIONIC CELLULOSE ETHERS FROM A SINGLE TREATMENT.**

In a 500 ml round bottom flask equipped with a mechanical stirrer, a nitrogen sparging tube, an addition funnel and a condenser was placed 141 grams of 2-propanol and 24 grams of water. To this

-22-

was added 30 grams of CELLOSIZE QP-4400 and the resulting slurry was purged for 1 hour with nitrogen. After 1 hour, 4.5 grams of a 20% NaOH solution was added and the mixture was stirred for an additional 30 minutes while purging with nitrogen. To this reaction was added 0.1% of QUAB 151 (based on the weight of the CELLOSIZE added) and the reaction was warmed to 55°C for 1 hour and kept at 55°C for an additional 90 minutes. The reaction was then cooled to 25°C and 2.4 grams of glacial acetic acid was added to neutralize the caustic. The reaction mixture was filtered through a Buchner funnel fitted with a #1 Whatman filter paper and the resulting solid product was reslurried in 300 mls of aqueous 2-propanol (of the same ratio as used in the reaction). The resulting product was refiltered and dried to afford the derivatized cellulose ether.

One gram of the resulting product was dissolved in 100 mls of distilled water and the resulting solution was placed into a Spectra/Por 7 dialysis membrane (available from the Spectrum company, Houston, TX) with a MWCO of 1000. The polymer was dialyzed against distilled water for three days with daily changes of the distilled water. The resulting solution was lyophilized to dryness and the resulting polymer analyzed for nitrogen using the Kjeldahl method. This particular sample had 0.4% cationic nitrogen. In a similar fashion, EXAMPLES

-23-

2-5 were run with 0.2, 0.65, 0.9 and 1.1% QUAB 151. The resulting corresponding percent nitrogen values are shown in Figure 1.

These Examples demonstrate that the addition of the aqueous QUAB 151 eventually results in a leveling off of the percentage of bound cationic nitrogen (indicative of the amount of reagent which reacts with the cellulose ether) and that treatments as high as 1.1% do not afford products with greater than 3.0% bound cationic nitrogen. The product from Example 3 is typical of the types of cationic cellulose ethers currently commercially available.

EXAMPLES 6-8 **PREPARATION OF CATIONIC CELLULOSE ETHERS FROM A** **DOUBLE TREATMENT**

Examples 6-8 were run exactly as described above for Examples 1-5 except that UCARE Polymer JR-400 with 1.8% cationic nitrogen (this product is similar to the material obtained from Example 3 above) already bound to the polymer was used as the starting material. In Example 6, 0.65% QUAB 151 was added to the reaction mixture based on the weight of the starting UCARE Polymer JR-400. In Example 7, 1.1% QUAB 151 was used, and in Example 8, 2.0% QUAB 151 was used. The data for the percent bound nitrogen for each of these Examples is shown in Figure 1.

In addition, the reaction mixture for Example 8, where 2.0% QUAB 151 was used, was isolated as a spongy swollen mass and was difficult to filter. This demonstrates that at QUAB 151 addition levels greater than 2.0%, one can expect that the reaction non-solvent (aqueous 2-propanol) will become sufficiently saturated with water as to begin swelling the cationic cellulose ether making the final product intractable.

Examples 6-8 again demonstrate that with increasing amounts of aqueous QUAB 151, a leveling effect occurs and percent of bound nitrogen values greater than 4.2 cannot be achieved even in a double treatment.

EXAMPLE 9
PREPARATION OF CATIONIC CELLULOSE ETHERS FROM A
TRIPLE TREATMENT

Example 9 was run using 0.65% QUAB 151 (based on the weight of the starting cationic cellulose ether) starting with the product obtained from Example 7 which was a double-treated cationic cellulose ether with a percent bound nitrogen of 3.9. The reaction was run exactly as described above for Examples 1-5. The resulting product obtained had 5.0% bound cationic nitrogen after the triple treatment as can be seen below in Figure 1.

EXAMPLE 10
PREPARATION OF HIGHLY CHARGED CATIONIC
HYDROXYETHYL CELLULOSE OF HIGHER MOLECULAR
WEIGHT

A sample of highly charged cationic cellulose ether was made using the process described in Example 1. This product was made by twice treating UCARE Polymer JR-30M using the process described in Example 1. The resulting product contained 3.6 % cationic nitrogen as determined by Kjeldahl analysis.

EXAMPLES 11-15
SHAMPOO APPEARANCE

Typical shampoos were made using the formulations shown in Table 1. The shampoos made with the cationic cellulose ethers of low charge were clear. The shampoos made from the highly charged cellulose ethers of the present invention appeared opaque.

Table 1.
Examples 11-15
Shampoo Formulations and Appearance
(Data appears as weight percent of ingredient)

Ingredient	Example 11	Example 12	Example 13	Example 14	Example 15
Ammonium Lauryl Sulfate	13.5	13.5	13.5	13.5	13.5
Sodium Laureth Sulfate	4.0	4.0	4.0	4.0	4.0
Cocamidopropylbetaine	3.0	3.0	3.0	3.0	3.0
Preservative	0.2	0.2	0.2	0.2	0.2
<i>Cationic Polymer: UCARE Polymer JR-400</i>	0.5	-	-	-	-

Table 1 (continued)

Ingredient	Example 11	Example 12	Example 13	Example 14	Example 15
<i>Cationic Polymer: UCARE Polymer JR-30M</i>	-	0.5	-	-	-
<i>Cationic Polymer: Example 7</i>	-	-	0.5	-	-
<i>Cationic Polymer: Example 10</i>	-	-	-	0.5	-
Water	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100	q.s. to 100
Appearance	Clear	Clear	Opaque	Opaque	Clear

EXAMPLES 16-17
WET COMBING STUDIES

Bleached blond hair tresses were washed using the shampoos described in Examples 11, 12, 13, 14 and 15. Example shampoos 11 and 13 contain polymers of similar molecular weight but different charge levels and Example shampoos 12 and 14 contain cationic polymers of similar molecular weights (higher than those found in Examples 11 and 13) but of different charge levels. Example 15 is a shampoo without cationic polymer. In each case, a five gram tress was washed with 0.2 grams of the shampoo for one minute, the tress was rinsed by dipping in 3 separate 600ml beakers of tap water 4 times and then combed briefly to align the fibers. Each tress was dipped five

-28-

times into a beaker containing 600 mls of tap water to allow slight but controlled entanglement of the hair fibers. The excess water was removed from the tress by squeezing with the fingers twice. The wet tress was placed onto a Miniature Tensile Tester Dia-Stronä and the force and energy required to pass the comb through the tress was measured. The results given as percentage combing force reduction are shown in Tables 2 and 3 below.

Table 2.
Combing Force results for Tresses
Prepared with Shampoo
Examples 11, 13 and 15.

Example #	2+ std	2- std	% Change
Example 11	64.6	25.2	44.9
Example 13	89.6	88.4	89
Example 15	48.5	11.1	29.8

Table 3.
Combing Force Results for Tresses
Prepared with Shampoo
Examples 12, 14 and 15.

Example #	2+ std	2- std	% Change
Example 12	80.5	73.7	77.1
Example 14	85.7	68.9	77.3
Example 15	48.5	11.1	29.8

EXAMPLES 18-19
CURL RETENTION STUDIES

Virgin Brown hair tresses all from a single batch of hair were cut to 27 cm length and prewashed with a shampoo containing only a non-ionic surfactant. A total of three tress samples per measurement were washed as described above for Examples 16-17 with shampoos from EXAMPLES 11, 12, 13 and 14. The resulting tresses were rinsed with warm water and rolled onto 1 inch curlers. The curled tresses were allowed to dry naturally overnight. The curlers were then gently removed from each curl, taking care not to damage the curled structure and the tresses were hung in a specially designed chamber which maintains the temperature at 20°C and the relative humidity at 90%. The tresses were then allowed to equilibrate in the chamber and the amount of curl droop was measured using a grid set behind the tresses. The results of the tress studies are shown below in Figures 3 and 4 which show the average percent of curl retention retained by each tress over a thirty minute time period. Table 4 shows the results for Example shampoos 11 and 13 and Table 5 shows the results from Example shampoos 12 and 14. In this way, polymers of similar molecular weight are compared to one another.

Table 4.
Percentage Curl Retention for Tresses
Prepared from Shampoo
Examples 11 and 13.

Example #	Time (min)				
	5	10	15	20	30
Example 11	67	52	45	43	39
Example 13	68	59	51	45	43

Table 5.
Percentage Curl Retention for Tresses
Prepared from Shampoo
Examples 12 and 14.

Example #	Time (min)				
	5	10	15	20	30
Example 12	70	54	44	40	39
Example 14	79	67	57	51	49

EXAMPLE 20
AQUEOUS VISCOSITY OF HIGHLY
CHARGED CATIONIC CELLULOSE ETHERS

One percent aqueous solutions of three commercially available cationic cellulose ethers, UCARE® Polymers LK-400, LR-400, and JR-400 and three highly charged cationic cellulose ethers of the present invention, EXAMPLE 6, EXAMPLE 7 and EXAMPLE 8 were examined for their viscosity verses shear rate behavior by using a Bohlin VOR Rheometer [Bohlin Instruments, Cranbury, NJ]. Measurements were taken using a C25 concentric cylinder geometry at 30°C. Each polymer has approximately the same molecular weight. The data for the measurements is shown in Figure 2.

-31-

In addition to the specific aspects of the invention described herein, those skilled in the art will recognize that other aspects are intended to be included within the scope of the claims which follow. For example, polysaccharides other than cellulose which can be derivatized with ether substituents and cationic substituent may be employed.

Claims:

1. A water-soluble, cationically modified cellulose ether characterized in that said cellulose ether comprises from about 1.5 to 6 moles of an ether substituent per mole of cellulose ether and is further substituted with a cationic substituent in an amount of at least about 3.0 wt % cationic substituent based on the total weight of the cellulose ether.
2. The cellulose ether of claim 1 wherein the cationic substituent comprises nitrogen.
3. The cellulose ether of claim 2 wherein cationic substituent is selected from the group consisting of alkyl substituted nitrogen compounds, aryl substituted nitrogen compounds and alkyl-aryl substituted nitrogen compounds.
4. The cellulose ether of claim 1 having a weight average molecular weight of from about 10,000 to 2,000,000 grams per gram mole.
5. The cellulose ether of claim 1 wherein the amount of cationic substituent is from about 3.0 to 8.0 wt % cationic substituent.
6. The cellulose ether of claim 1 wherein the cellulose ether is selected from the group consisting of hydroxyethyl cellulose, hydroxypropyl cellulose, methyl cellulose, hydroxypropyl methyl cellulose, hydroxyethyl methyl cellulose, hydroxyethyl carboxymethyl cellulose and mixtures thereof.

7. The cellulose ether of claim 6 wherein the cellulose ether is hydroxyethyl cellulose.

8. A personal care composition containing a water-soluble, cationically modified cellulose ether according to claim 1 and at least one personal care ingredient.

9. A method for manufacturing a cationically modified cellulose ether comprising:

(i) reacting a cellulose ether with a first aqueous cationizing reagent to form a first reaction product comprising a first cationic cellulose ether and water;

(ii) removing at least a portion of the water from the first reaction product to form a dried reaction product comprising the first cationic cellulose ether; and

(iii) reacting the dried reaction product with a second aqueous cationizing reagent to form a second reaction product comprising a second cationic cellulose ether having a higher substitution level of cationic substituent than the first cationic cellulose ether.

10. The method of claim 9 wherein the first cationic cellulose ether has a cationic substitution level of less than about 2.5 wt % cationic substituent based on the total weight of the cellulose ether.

11. The method of claim 9 wherein the second cationic cellulose ether has a cationic substitution level of at least about 3.0 wt % cationic substituent based on the total weight of the cellulose ether.

12. The method of claim 9 wherein the dried reaction product comprises from about 0.1 to 50 wt % water based on the total weight of the dried reaction product.

Figure 1.

Percent bound nitrogen verses percent epoxide treatment level for single (◆, EXAMPLES 1-5), double (■, EXAMPLES 6-8) and triple (●, EXAMPLE 9) treatments with 70% aqueous QUAB 151.

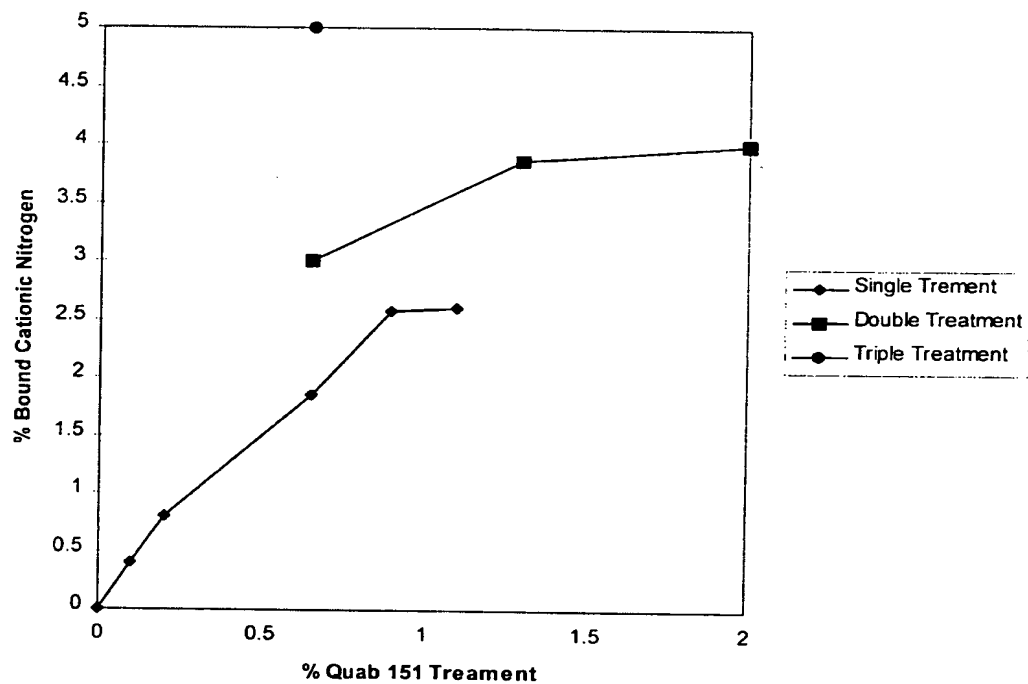
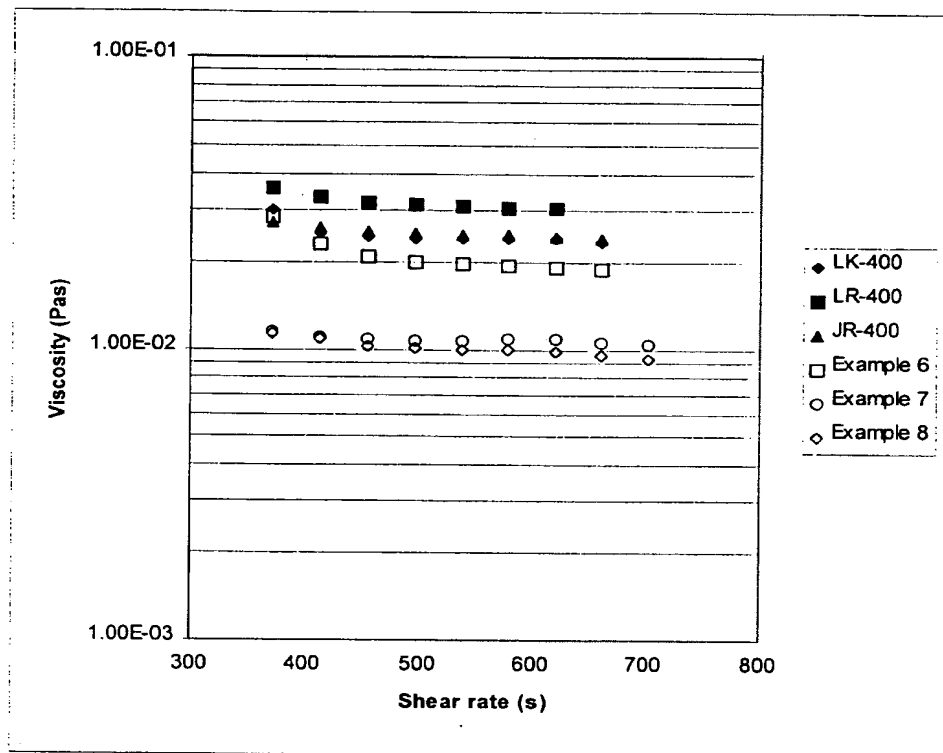


Figure 2.

Viscosity verses shear rate for 1.0 % aqueous solutions of three commercially available cationic cellulose ethers (UCARE® Polymers LK-400, LR-400 and JR-400) and cationic cellulose ethers from Examples 6, 7 and 8.



INTERNATIONAL SEARCH REPORT

Intern: al Application No

PCT/US 00/35615

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C08B11/193 A61K7/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C08B A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 614 616 A (HANS-JOSEF BUYSCH) 25 March 1997 (1997-03-25) column 4, line 31 - line 33 examples 3-5	1-8
X	US 4 220 548 A (SHIGERU HASHIMOTO ET AL.) 2 September 1980 (1980-09-02) column 2, line 58 - line 64 column 4, line 14 - line 26	1-8
Y	PATENT ABSTRACTS OF JAPAN vol. 12, no. 301 (C-521), 16 August 1988 (1988-08-16) & JP 63 072701 A (DAICEL CHEMIND LTD), 2 April 1988 (1988-04-02) abstract	1-8

-/--

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

5 April 2001

Date of mailing of the international search report

02/05/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Lensen, H

INTERNATIONAL SEARCH REPORT

Intern: .al Application No
PCT/US 00/35615

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>PATENT ABSTRACTS OF JAPAN vol. 5, no. 128 (C-067), 18 August 1981 (1981-08-18) & JP 56 062801 A (KAO CORP), 29 May 1981 (1981-05-29) abstract & DATABASE WPI Week 198129 Derwent Publications Ltd., London, GB; AN 1981-52253D</p> <p>-----</p>	1-8

INTERNATIONAL SEARCH REPORT

Information on patent family members

Intern: al Application No

PCT/US 00/35615

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5614616 A	25-03-1997	DE 4026617 A DE 59107274 D EP 0472075 A FI 913953 A	27-02-1992 29-02-1996 26-02-1992 24-02-1992
US 4220548 A	02-09-1980	JP 1251605 C JP 53140305 A JP 58049595 B FR 2387031 A	14-02-1985 07-12-1978 05-11-1983 10-11-1978
JP 63072701 A	02-04-1988	JP 7072201 B	02-08-1995
JP 56062801 A	29-05-1981	NONE	